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10/572,795	10/09/2008	Thomas Wilckens	3724-101	4240

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EXAMINER	
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ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
11/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/572,795	WILCKENS ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-45* is/are pending in the application.

4a) Of the above claim(s) *32,34-38,43,44 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-31,33,39-42 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/21/06; 9/3/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 28-31, 33, 39-42 and 45-46) in the reply filed on October 4, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant further elects glycyrrhetinic acid as the species election.

Claims 32, 34-38, 43-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 4, 2010.

Status of Claims

2. Claims 28-46 are pending and claims 28-31, 33, 39-42 and 45-45 are under examination based on the response to the restriction requirement mailed 8/6/10. Claim 46 do not recite the elected species, therefore it has been withdrawn by the Examiner.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 3/16/07 is acknowledged and has been reviewed.

Priority

4. Acknowledgement is made of the present application as a National Stage (371) entry of PCT Application No. PCT/EP05/10582, filed September 21, 2004, which claims benefit under 35 U.S.C. 119(e) to U.S. Provisional Patent Application No. 60/504,717, filed September 22, 2003.

Claim Objections

5. Claim 45 are objected to because of the following informalities: The abbreviation 11 β-HSD type 1 should be given as its full name or with the full name in parenthesis therewith when first used. Appropriate correction is required.

6. The formula structures of claim 33 should be drawn correctly for better interpretation. Applicant should also correct any other structural deficit with regards to the formulae in the specification and the claims. For example the bonds should be drawn to point of attachment to the molecule (see Formulae16, 25).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31, 33, 39-42 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating peridonitis, does

not reasonably provide enablement for preventing periodonitis inflammatory induced and/or immune-mediated loss of bone and/or other cartilage as recited in instant claim 28. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, sufficient amounts for a prima facie case are discussed below.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth infra.

The nature of the invention. The invention discloses using 11β HSD type 1 for prevention or treatment of periodontal diseases.

The State of the Prior Art. The prior art discloses that using glycyrrhetinic acid treats periodontal disease.

The Predictability or Lack Thereof in the Art. Prevention is not practical with oral diseases due to the unpredictability of the condition. According to Socrasky bacterial periodontal disease is unique in that if the bone supporting the tooth is lost destruction of the bone would average 1mm/year, it is also faced with studying the bacterial etiology of periodontal disease and when coupled with the complexity of the microbiota, it becomes difficult to assign an etiology role to any organism, coupled with lack of good animal model thus making prevention very difficult (see entire article). The calculus, if untreated, causes gingivitis, the first stage of periodontal disease (see PeridontalGum_Eng.pdf. Therefore it is likely a small amount of gingivitis is present in between dental visits. In the case of the instant invention, periodontal disease can be caused by different factors, therefore it is nearly impossible to protect against them all with one compound.

The Amount of Direction or Guidance Present. The disclosure teaches that the composition may be used to reduce inflammation of periodontal disease but does not show the effects of the composition when the teeth are free of bacteria that leads to periodontal disease.

The Presence or Absence of Working Examples. The examples present in the specification are a representation of the effect a composition on the formation of periodontal disease. There is a lack of examples showing the effect of the composition

on the development of periodontal disease over a long period of time or how long the effects of the compositions last before periodontal diseases forms.

The Breadth of the claims. The claims are broad because they read on "prevention".

Suggested language. Since the term "treatment" is a broad term, it will inherently cover therapies in which some protective function may also be present. Accordingly, the examiner recommends simply reciting method for "treatment" of periodontal diseases.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Even though a specie election was made the claims as recited are broad and do not recite specifically the elected species. Therefore the below rejection is made.

Claims 28-31, 39, 41-42 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Ramakrishnam (US 2003/0148349).

Ramakrishnam teaches a method of treating (see para 0195) osteoporosis and osteoarthritis (loss of bone mass (see 0197 and 0207, as required by instant claim 31) comprising the step of administering a pharmaceutical composition comprising an active agent 11 β HSD type 1 (as required by instant claims 28 and 45, see 0194) wherein the patient may be a mammal and a human (as required by instant claims 29-30). Additionally Ramakrishnam teaches that the active agent may be in combination with at least one other active agent (see para 0185, as required by instant claim39 that may be administered oral (as required by instant claims 41-42, see 0189)

Therefore Ramakrishnam anticipates the claimed invention of instant claims 28-31, 39, 41-42 and 45.

9. Claims 28-31, 33, 39, 41-42 and 45-46 are rejected under 35 U.S.C. 102(e) as being anticipated by Ruggles (US Patent 2005/0048007).

Ruggles teach a method of treating periodontal disease (see 0008-0009, as required by instant claims 28 and 31) comprising orally administration (as required by instant claims 41-42) of an extract *glycyrrhino glabra* (i.e., constitutes glycyrrhetinic acid (see 0012, as required by instant claims 28, 33 and 45) to humans and animals/mammals (as required by instant claims 29-30). Ruggles further teaches that the treatment composition may further comprise other active agents (see 0019, as required by instant claim 39).

Therefore Ruggles anticipates instant claims 28-31, 33, 39, 41-42 and 45.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 28-30, 33 and 45 rejected under 35 U.S.C. 102(b) as being anticipated by Baxendale et al. (DE 2840259A).

Baxendale teaches a method of treating inflammatory diseases comprising administering a formulation comprising a 11 β-HSD type 1 inhibitor (glycyrrhetinic acid) in a pharmaceutically acceptable salt (as required by instant claims 28, 33 and 45, see abstract English translation). Because Baxendale teaches treatment of inflammatory disease, it is expected that the treatment would be administered to mammals and humans (absent factual evidence to the contrary, as required by instant claims 29-30).

Therefore Claims 28-31 and 45 are anticipated by Baxendale et al.

11. Claims 28-31, 39, 41-42 and 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Ramakrishnam (WO 2002/02797).

Ramakrishnam teaches a method of treating (see page 47, lines 28-30) osteoporosis and osteoarthritis (loss of bone mass; see page 48, lines 19-20, as required by instant claims 31 and 46) comprising the step of administering a pharmaceutical composition comprising an active agent 11 β HSD type 1 (as required by instant claims 28 and 45, see page 47, lines 28-30) wherein the patient may be a mammal (as required by instant claims 29-30). Additionally Ramakrishnam teaches that the active agent may be in combination with at least one other active agent (see page

45, lines 5-14, as required by instant claim 39 that may be administered oral (as required by instant claims 41-42, see45, lines 19-22)

Therefore Ramakrishnam anticipates the claimed invention of instant claims 28-31, 39, 41-42 and 45-46.

Claims 28-31, 39 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Braden et al. (US Patent 5,468,787).

Braden et al. teach a method of treating (i.e., promoting) repair cartilage comprising the use of marcropolymer incorporated with a 11-β-HSDtype 1 drug (i.e., dexamethasone, as required by instant claims 28, 31 and 45, when the specification is used as a guideline see page 25) wherein the composition comprises other active agent (as required by instant claim 39, see col. 2, lines 40-55) to mammals (i.e., animals and humans, as required by instant claim 29-30 (see 6, lines 28-30).

Therefore Branden anticipates claims 28-31, 39 and 45.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-31, 33, 39-42, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruggles (US Patent 2005/0048007) in view of Kiso (JP 07291857, see English Abstract) and further in view of Jeffcoat et al. J. Peridontal (1980) 51(10) 599-602 (abstract Only).

Ruggles teach a method of treating periodontal disease (see 0008-0009, as required by instant claims 28 and 31) comprising orally administration (as required by instant claims 41-42) of an extract *glycyrrhino glabra* (i.e., constitutes glycyrrhetinic acid (see 0012, as required by instant claims 28, 33 and 45) to humans and

animals/mammals (as required by instant claims 29-30). Ruggles further teaches that the treatment composition may further comprise other active agents (see 0019, as required by instant claim 39).

However Ruggles fails to teach the dosage amount of glycyrrhetinic acid as required by instant claim 40.

Kiso teaches treating osteopathy comprising administering the therapeutic composition of glycyrrhetinic acid (salt) as the active agent in a daily dose of 0.1-10 mg/Kg which is within the dosage amount required by instant claim 40.

However Kiso fails to teach specifically treating periodontal disease.

Jeffcoat et al. teach periodontal disease is a bone disease.

Nonetheless it is known in the art and to one of ordinary skill in the art that periodontal disease is a disease that affects the bone (absent factual evidence).

Ruggles teaches that the composition may comprise 0.47%-63% of glycyrrhetinic acid by weight, therefore one of ordinary skill in the art would be motivated to substitute the dosage form of Ruggles for Kiso's dosage form for the treatment of periodontal disease with a reasonable amount of success because it is know in the art that periodontal disease is a bone disease as taught by Jeffcoat et al. (see abstract). Therefore one of ordinary skill in the art would have been motivated to combine Ruggles with Kiso to result in the claimed invention at the time the invention was filed.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1628

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628